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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,034	10/02/2003	Jeffrey C. Rapp	AVI-034CIP	1081

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AVIGENICS, INC.
111 RIVERBEND ROAD
ATHENS, GA 30605

EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	
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09/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/679,034	RAPP ET AL.
	Examiner	**Art Unit**
	Michael C. Wilson	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2007*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.
4a) Of the above claim(s) *32-52* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-31* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date *9-21-04&1-16-07*.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-52 remain pending.

Applicants are reminded that for ease of examination, amending existing claims with underlining and bracketing is preferred over canceling existing claims then adding similar new claims.

The introductory paragraph of applicants' response should provide support for all limitations in amendments by page and line number.

Applicants' response should have headings for each rejection followed by arguments for each rejection.

Specification

This application still fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: The sequences in the specification and Drawings have inconstancies. SEQ ID NO: 6 in Fig. 1 is not the same as SEQ ID NO: 6 in Fig. 15. SEQ ID NO: 5 in Fig. 2 is not the same as SEQ ID NO: 5 in Fig. 15. None of the SEQ ID NOs in Fig. 1-6 and 14 correlate to the SEQ ID NOs in Fig. 15. In addition, SEQ ID NO: 42 (claim 16 and 30) does not exist. Applicants must file a "Sequence Listing" accompanied by directions to enter the listing into the specification as an amendment. Applicant also must provide statements regarding sameness and new matter with regards to the CRF and the "Sequence Listing." Failure to fully comply with the sequence rules in response to the instant office action will be considered non-responsive.

The application contains patent application numbers that will have to be updated upon being allowed or abandoned (e.g. pg 24, pg 92, pg 96).

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-31, in the reply filed on 8-24-07 is acknowledged.

Claim Rejections - 35 USC § 112

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing transgenic avians comprising microinjecting into a cell of an avian embryo a nucleic aicd comprising a transgene comprising a nucleotide sequence encoding a heterologous polypeptide; introducing the microinjected avian embryo into an oviduct of a recipient hen, such that the recipient hen lays a shelled egg containing the microinjected avian embryo; incubating the shelled egg containing the microinjected avian embryo until the egg hatches; testing a hatched chick for the presence of the transgene; and developing a chick that tests positive for the transgene to sexual maturity does not reasonably provide enablement for making a transgenic avian by merely incubating a shelled egg containing the microinjected avian embryo until hatch, using any "tissue-specific promoter" or "magnum-specific promoters," a "heterologous polypeptide... ...optimized for codon usage by an avian," a transgene comprising "at least two nucleotide sequences each encoding a heterologous polypeptide," "that form a multimeric protein," that "specifically bind a selected ligand," that is an "antibody," for using BAC to obtain transgenic avians. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1 is directed toward making a transgenic avian by microinjecting a nucleotide sequence into an avian embryo or germinal disc to produce a transgenic avian. The claims encompass making germline and non-germline transgenic avians.

Please provide a copy of the Declaration by Dr. Christmann and the Declaration by Dr. Leavitt filed in parent application 10/251364 regarding making transgenics in species other than chickens.

Methods of making transgenic chickens by injecting vectors or cells transfected with vectors into chicken embryos were known in the art:

Stage XI PGCs had been isolated from chickens, transduced with retrovirus, and immediately injected into the vasculature of Stage 15 chick embryos to obtain germline transmission of a transgene (Vick, Proc. R. Soc. Lond., 1993, Vol. 251, pg 179-182).

Love taught microinjecting plasmid DNA into the germinal disc of chick zygotes (Stage I); the zygotes were maintained in host shells in vitro until hatch. Germline transmission of the transgene was obtained (Love, Bio/Technology, 1994, Vol. 12, pg 60-63).

Tanaka (1994, J. Reprod. Fert., Vol. 100, pg 447-449) placed sperm on a fertilized an chicken ovum that had been removed from its shell and placed in culture medium (pg 447, col. 2, "Materials and Methods"; pg 448, Fig. 1) The day old fertilized ovum was transferred into the birth canal of a recipient hen. A shell formed around the fertilized ovum as it passed through the recipient hen's reproductive system, the egg was laid on the day following the transfer (pg 448, col. 1, line 4) and a chick hatched (pg 448, col. 2, first full ¶, line 9). Tanaka did not teach the plasmid DNA was microinjected into a one-celled embryo.

Thoraval injected retroviral vectors into the subgerminal cavity of an avian embryo in a freshly laid egg using a glass capillary and obtained germline transmission of the transgene (Thoraval, Transgenic Research, 1995, Vol. 4, pg 369-376).

Sayegh introduced a retroviral vector encoding a truncated antibody receptor into chickens "somatically" and express the receptor in the bursa at hatch (Sayegh, Dec. 15, 1999, Vol. 72, pg 31-37; pg 32, 2nd full ¶, lines 2-5 and 16-18; ¶ bridging pg 33-34).

Mohammed (1998, Immunotechnology, Vol. 4, pg 115-125), taught that although using hens for the production of recombinant human antibodies (rhAb) has been discussed, it had never been demonstrated. Mohammed transfected a lymphoblastoid cell line with a retrovirus encoding a rhAb, injected the cells into a chicken and obtained expression of the rhAb in the egg yolk and sometimes the egg white (pg 116, col. 1, 2nd ¶; col. 2, 1st full ¶). The method of Mohammed is not a method of transgenesis because the transfected cells were not integrated into the germline of the chicken. Only the exogenous lymphoblastoid cell line taught by Mohammed expressed the exogenous protein in the chicken.

Ishida (2002, Cloning Stem Cells, Vol. 4, pg 91-102) suggested making chickens expressing human antibodies but did not teach how to make transgenic chickens (see abstract).

Harvey (Nature Biotech, April 2002, Vol. 19, pg 396-399) taught making transgenics by injecting a retroviral vector encoding beta-lactamase operably linked to the CMV promoter into the subgerminal cavity of stage X embryos. The chicks produced exogenous protein in their eggs (pg 397, col. 2, 2nd full ¶).

Ivarie (Trends in Biotechnology, Jan. 2003, Vol. 21, pg 14-19), taught that because of the complex process by which a bird makes and lays eggs, transgenic procedures for birds have lagged far behind those of other organisms. Ivarie cites Pain who taught long-term culture of non-transfected, blastodermal cells that provided germline transmission; however, no transgenic birds have been made using transfected ES cells or PGCs. The biggest obstacle to overcome in making transgenic birds using transfected ES cells or PGCs is the loss of germline competence during culture of transfected ES cells and PGCs (pg 14, col. 2, 3rd full ¶, 1st sentence; pg 17, col. 1, 2nd full ¶, last two sentences; pg 17, sentence bridging col. 1-2; pg 17, col. 2, last sentence).

Naito (Transgenic Animals: Generation and Use, 1997, Ed. By Louis Marie Houdebine, Harwood Academic Publishers, pg 69-73) summarizes the microinjection of DNA into early chicken embryos (pg 70-71, "Microinjection of DNA"; pg 71, Fig. 14.4

"DNA microinjection into the germinal disc of fertilized ovum at the single stage"). Love is cited by Naito on pg 72, col. 1, last full paragraph, and cites the work of Love delivered DNA to a stage I chicken zygote, allowed the zygote to become a chick and obtained transgenic chicks.

The specification does not enable merely incubating a shelled egg containing a microinjected avian embryo until the shelled egg hatches. The only disclosed use for the method is to obtain a transgenic avian from the hatched egg. Which should be clearly set forth in the claim.

The specification does not enable any "tissue specific promoter" or "specific for the magnum" as claimed (6, 7). The specification defines a "magnum-specific" promoter as "a promoter that is primarily or exclusively active in the tubular gland cells of the avian magnum (pg 13, paragraph 42). No such promoters have been described in the specification. The CMV promoter and lysozyme promoter described by Harvey, Ivarie and Love, for example were constitute promoters and did not cause expression "primarily or exclusively" in tubular gland cells or magnum. Without such guidance and in view of the absence of such promoters in the art or the specification, it would have required one of skill undue experimentation to isolate such promoters. Deletion of this aspect of the claims would overcome this rejection.

The specification does not enable using BAC expression vectors to make transgenic avians (claims 15, 16, 29 and 30). The art at the time of filing was limited to making transgenic chickens using plasmids or viral vectors. While BAC vectors were known in the art for use in manipulating large genomic sequences (pg 44, last part of paragraph 75), it was unknown whether BAC vectors would stably transfect chicken embryos such that transgenic chickens were obtained. The specification does not correlate the difference in size of the BAC vectors with plasmids or viral particles known in the art to successfully produce transgenic chickens. Without such guidance and in view of the lack of correlation between plasmids and viral particles known in the art capable of producing transgenics and BAC vectors, it would have required one of skill undue experimentation to use BAC promoters to obtain transgenic chickens because BAC vectors may not work. Cancellation of claims 15, 16, 29 and 30 is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the method steps merely require hatching a microinjected avian embryo but does not result in a chick comprising the transgene. The claim should clearly set forth obtaining a chick that comprises the transgene.

Claim 2 is indefinite because the metes and bounds of an "early stage" embryo cannot be determined. One of skill would not be able to determine which stages applicants consider "early" stages of development.

Claim 3 is indefinite because the metes and bounds of a developing egg cannot be determined. In particular, it is unclear when an egg is no longer "developing." Deleting "developing" would overcome this rejection.

Claim 6 is indefinite because the metes and bounds of a "tissue specific promoter" are not defined in the specification or the art at the time of filing.

Claim 7 is indefinite because the metes and bounds of a "tissue specific promoter" "specific for the magnum" are not defined in the specification or the art at the time of filing.

Claim 8 is unclear because it cannot be determined how the nucleotide sequence is associated with an NLS during microinjection. The nucleotide sequence may comprise a nucleic acid sequence encoding an NLS but it is not combined with an NLS peptide prior to microinjection as claimed.

Claim 9 is indefinite because the metes and bounds of a coding sequence that is "optimized for codon usage by an avian" are unclear. The metes and bound of such coding sequences cannot be envisioned. In particular, the structure of such coding sequences and the process used to optimize such coding sequences cannot be envisioned.

Claim 16 is indefinite because use of the parentheses makes the claim unclear. In particular, it is unclear if SEQ ID NO: 42 is included in the claim. Furthermore, the sequence listing does not include SEQ ID NO: 42.

Claims 16 and 17 are indefinite because "a heterologous polypeptide-encoding sequence" in claim 16 does not further limit the heterologous polypeptide in claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 11 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka (1994, J. Reprod. Fert., Vol. 100, pg 447-449) in view of Naito (Transgenic Animals: Generation and Use, 1997, Ed. By Louis Marie Houdebine, Harwood Academic Publishers, pg 69-73) and Love (Bio/Techn., Jan. 12, 1994, Vol. 12, pg 60-63).

Tanaka delivered plasmid DNA encoding β-actin and LacZ to a zygote before delivering the zygote to the oviduct of a recipient hen (pg 449, col. 1, last ¶; pg 447, first paragraph). The zygote hatched and became a chick (pg 447, col. 2, "Materials and Methods;" pg 448, Fig. 1; pg 448, col. 1, line 4; pg 448, col. 2, 1st full ¶, line 9). Tanaka did not teach the plasmid was delivered by microinjection as in claim 1, specifically into an embryo having a germinal disc as in claim 2.

However, Naito delivered plasmid DNA to a stage I chicken zygote and allowed the zygote to become a chick (pg 70-71, "Microinjection of DNA"; pg 71, Fig. 14.4 "DNA microinjection into the germinal disc of fertilized ovum at the single stage"). Love is cited by Naito on pg 72, col. 1, last full paragraph, who also described microinjecting the germinal disc of zygotes (Stage I) and obtaining transgenic avians.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver DNA to a zygote, deliver the zygote into the birth canal of a hen and allow the zygote to become a chick as taught by Tanaka wherein the DNA was delivered using the microinjection technique taught by Naito and Love. One of ordinary skill in the art at the time the invention was made would have been motivated to deliver the DNA of Tanaka using the technique described by Naito and Love because

Naito and Love described how to obtain transgenic chickens.

The technique described by Naito and Love inherently results in delivery of the white of a developing avian egg made by the transgenic avian (claim 3).

The phrases "tissue specific" and "specific for the magnum" (claims 6 and 7) are not defined in the specification or the art at the time of filing; therefore, the phrases encompass any promoter that causes expression. The promoter described by Tanaka causes expression in all tissues including the magnum (pg 61, Fig. 1B), thus meeting the limitations of claims 6 and 7.

Claim 8 is included because a nucleic acid sequence cannot comprise a peptide.

Claim 9 is included because the metes and bounds of a coding sequence that is "optimized form codon usage by a chicken" are unclear.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-14, 18-22, 25-27 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ivarie (US Patent 6,730,822) in view of Tanaka (1994, J. Reprod. Fert., Vol. 100, pg 447-449).

Ivarie produced exogenous interferon alpha or erythropoietin protein in an egg of a chicken, which method comprises: a) providing an avian leukosis viral vector comprising a nucleic acid sequence encoding an exogenous interferon alpha or erythropoietin protein, and a constitutive promoter operably linked to said sequence, wherein said promoter drives expression of the encoding sequence in the chicken oviduct; b) introducing said vector into chicken stage X embryonic cells; c) incubating said embryonic cells under conditions conducive to hatching live chicks; d) nurturing growth of a mature chimeric chicken from said chicks; e) mating said chimeric chicken, either naturally or via artificial insemination, with a non-transgenic chicken; f) identifying a transgenic chicken by screening the progeny of step e) for germ line incorporation of the protein encoding sequence; and g) mating the transgenic progeny with non-transgenic chickens to produce eggs containing the exogenous protein (claim 1). The protein could be extracted from the egg (claim 4 of Ivarie). The virus was microinjected as claimed because it was introduced using a glass capillary (col. 20, lines 45-50 of '822 states the virus was injected using the method of Thoraval; Thoraval teaches injecting virus into the embryo using a glass capillary on pg 370, col. 2, 2nd full ¶). The virus had a CMV promoter (col. 19, Ex. 1). The offspring produced exogenous protein in their serum and egg white (Examples 4 and 5). The virus was injected into the subgerminal cavity (Thoraval, pg 370, col. 2, 2nd full ¶), which is equivalent to injecting the "germinal disc" as claimed because the subgerminal cavity is below the germinal disc and is accessed by injecting the germinal disc. Ivarie did not teach the embryos were introduced into an oviduct of a recipient hen.

However, Tanaka taught delivering DNA to an embryo, then delivering the embryo to the oviduct of a recipient hen (pg 449, col. 1, last ¶). The embryo hatched and became a chick (pg 447, col. 2, "Materials and Methods;" pg 448, Fig. 1; pg 448, col. 1, line 4; pg 448, col. 2, 1st full ¶, line 9).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver virus encoding an exogenous protein under the control of the CMV promoter into an embryo by glass capillary and allow the embryo to become a chick as taught by Ivarie wherein the embryo was introduced into a recipient hen's oviduct as described by Tanaka. One of ordinary skill in the art at the time the invention was made would have been motivated to transplant the embryo of Ivarie into the oviduct of a recipient hen to provide the most natural environment for the embryo and to avoid artificial methods of incubating the embryo in media in a host shell.

The Stage X embryo described by Ivarie is an "early stage embryo" (claim 1) because the metes and bounds of what applicants consider early are unclear (see 112/2nd).

The virus could also have the Ovalbumin promoter (Fig. 2A; Fig. 2C; Fig. 6B) (claim 64).

The technique described by Ivarie inherently results in expression, specifically in the magnum, because the CMV promoter is a constitutive promoter and because cells in the magnum had the transgene in their genome (col. 8, lines 4-10).

The CMV promoter is a "tissue specific promoter" (claim 6) because it provides expression of the exogenous protein in the egg white and serum.

The CMV promoter is a promoter "specific for magnum tissue" (claim 7) because it is provides expression of the exogenous protein in the egg white and meets the definition of "magnum-specific" in col. 15, lines 48-52, of Ivarie and because cells in the magnum had the transgene in their genome (col. 8, lines 4-10).

Claim 9 is included because the metes and bounds of a coding sequence that is "optimized form codon usage by a chicken" are unclear.

Claims 10 and 31 are included because the virus of Ivarie had an IRES (Fig. 2F).

Claims 12, 25 and 26 are included because the virus of Ivarie encoded neo and gene X (Fig. 2A and 2F).

Claims 14 and 28 are included because Ivarie taught the vector could encode an antibody (col. 19, lines 24-42).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-7, 9, 11-13, 19-22 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harvey (Nature Biotech., April 2002, Vol. 19, pg 396-399) in view of Tanaka (1994, J. Reprod. Fert., Vol. 100, pg 447-449).

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-31 of this application. Provisional application 60/351550 (1-25-02) does not teach microinjecting a transgene into any avian embryo or introducing the embryo into the oviduct of a recipient hen as currently claimed. The microinjection step in '550 is limited to microinjecting plasmid into the germinal disc of stage I chicken embryos. '550 states:

> "Approximately two nanoliters of DNA were injected into the germinal disk of stage I (E,G.&K,) White Leghorn embryos obtained two hours after oviposition of the previous egg. DNA amounts per injection ranged from 10 picograms to 400 picograms. Injected embryos were surgically transferred to recipient hens, and hard shell eggs were incubated and hatched..." (pg 2 of 343; 2nd ¶).

'550 did not teach transferring the embryo into the oviduct; therefore, the effective filing date of the claims is 9-18-02 – the filing date of application 10/251364.

Harvey produced an exogenous beta-lactamase in an egg white of a chicken by injecting retrovirus encoding the protein under the control of the CMV promoter into the subgerminal cavity of stage X chick embryos, incubating embryos and hatching live chicks that produced the protein in their egg whites (pg 397, col. 2, 2nd full ¶). Harvey describes the eggs are bioreactors (pg 398, last ¶), which means the protein is isolated from the egg white. The retrovirus of Harvey was microinjected as claimed because only 7-10 microliters were injected. Injection into the subgerminal cavity as taught by Harvey is equivalent to injecting the "germinal disc" (claim 2) because the subgerminal cavity is below the germinal disc and is accessed by injecting the germinal disc. Harvey did not teach the embryos were introduced into an oviduct of a recipient hen.

However, Tanaka (1994, J. Reprod. Fert., Vol. 100, pg 447-449) taught delivering DNA to an embryo, then delivering the embryo to the oviduct of a recipient hen (pg 449, col. 1, last ¶). The embryo hatched and became a chick (pg 447, col. 2, "Materials and Methods;" pg 448, Fig. 1; pg 448, col. 1, line 4; pg 448, col. 2, 1st full ¶, line 9).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver virus encoding an exogenous protein under the control of the CMV promoter into an embryo and allow the embryo to become a chick as taught by Harvey wherein the embryo was introduced into a recipient hen's oviduct as described by Tanaka. One of ordinary skill in the art at the time the invention was made would have been motivated to transplant the embryo of Harvey into the oviduct of a recipient hen to provide the most natural environment for the embryo and to avoid artificial methods of incubating the embryo in media in a host shell.

The Stage X embryo described by Harvey is an "early stage embryo" (claim 2) because the metes and bounds of what applicants consider early are unclear (see 112/2nd).

The CMV promoter is a "tissue specific promoter" (claim 6) because it provides expression of the exogenous protein in the egg white.

The CMV promoter is a promoter "specific for magnum tissue" (claim 7) because it is provides expression of the exogenous protein in the egg white.

Claim 9 included because the metes and bounds of a coding sequence that is "optimized form codon usage by a chicken" are unclear.

Claims 11-13 and 25-27 are included because the virus of Harvey encoded neo and beta-lactamase (Fig. 1A).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 and 18-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of copending Application No. 10/251364 in view of the disclosure of '364. ''364 claims a method of producing a transgenic avian comprising microinjecting into a cell of an avian embryo a nucleic acid comprising a transgene comprising a nucleotide sequence encoding a heterologous polypeptide; introducing the microinjected avian embryo into an oviduct of a recipient hen, such that the recipient hen lays a shelled egg containing the microinjected avian embryo; incubating the shelled egg containing the microinjected avian embryo until the egg hatches; testing the a hatched chick for the presence of the transgene; and developing a chick that tests positive for the transgene, to sexual maturity. The subject matter now claimed in the instant application but not claimed in '364 is in the disclosure of '364. Thus, it would have been obvious to perform the method claimed in '364 using the limitations now claimed. This is a provisional obviousness-type double patenting rejection.

Claims 1-15 and 18-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/842606 in view of the disclosure of '606. '606 claims a method of producing a transgenic avian comprising: delivering a nucleic acid solution to oviduct tissue of an avian by administering the nucleic acid solution to an artery or a vein which supplies blood to the oviduct tissue wherein the administration is under pressure and wherein the nucleic acid solution is delivered under pressure to oviduct tissue and the nucleic acid enters a cell of the oviduct tissue and is expressed, thereby producing a transgenic avian. The subject matter now claimed in the instant application but not claimed in '606 is in the disclosure of '606. Thus, it would have been obvious to perform the method claimed in '606 using the limitations now claimed. This is a provisional obviousness-type double patenting rejection.

Claims 1-15 and 18-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 11/337361 in view of the disclosure of '361. '361 claims a method comprising recovering from an avian egg a protein wherein the protein is exogenous to the egg. The subject matter now claimed in the instant application but not claimed in '361 is in the disclosure of '361. Thus, it would have been obvious to perform the method claimed in '361 using the limitations now claimed. This is a provisional obviousness-type double patenting rejection.

Claims 1-15 and 18-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 11/376023 in view of the disclosure of '023. '023 claims a method comprising recovering from an avian egg a protein wherein the protein is exogenous to the egg. The subject matter now claimed in the instant application but not claimed in

'023 is in the disclosure of '023. Thus, it would have been obvious to perform the method claimed in '023 using the limitations now claimed. This is a provisional obviousness-type double patenting rejection.

Claims 1-14 and 19-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,730,822 (US Application 10/, in view of the disclosure of '822, and Tanaka (1994, J. Reprod. Fert., Vol. 100, pg 447-449). '822 claimed a method for producing an exogenous interferon alpha or erythropoietin protein in an egg of a chicken, which method comprises: a) providing an avian leukosis viral vector comprising a nucleic acid sequence encoding an exogenous interferon alpha or erythropoietin protein, and a constitutive promoter operably linked to said sequence, wherein said promoter drives expression of the encoding sequence in the chicken oviduct; b) introducing said vector into chicken stage X embryonic cells; c) incubating said embryonic cells under conditions conducive to hatching live chicks; d) nurturing growth of a mature chimeric chicken from said chicks; e) mating said chimeric chicken, either naturally or via artificial insemination, with a non-transgenic chicken; f) identifying a transgenic chicken by screening the progeny of step e) for germ line incorporation of the protein encoding sequence; and g) mating the transgenic progeny with non-transgenic chickens to produce eggs containing the exogenous protein (claim 1). The protein could be extracted from the egg (claim 4 of '822). '822 did not claim the virus was microinjected, the virus had a CMV promoter, the offspring produced exogenous protein in their magnum or egg white, or that the nucleic acid was injected into the germinal disc.

However, '822 taught the many other limitations currently claimed that could have been claimed in '822 based on the disclosure of '822. The virus of '822 was microinjected as claimed because it was introduced using a glass capillary (col. 20, lines 45-50 of '822 states the virus was injected using the method of Thoraval; Thoraval teaches injecting virus into the embryo using a glass capillary on pg 370, col. 2, 2nd full ¶). The virus had a CMV promoter (col. 19, Ex. 1). The offspring produced exogenous protein in their egg white (Examples 4 and 5). The virus was injected into the subgerminal cavity (Thoraval, pg 370, col. 2, 2nd full ¶), which is equivalent to injecting the "germinal disc" as claimed because the subgerminal cavity is below the germinal disc and is accessed by injecting the germinal disc. The Stage X embryo described by Ivarie is an "early stage embryo" (claim 2) because the metes and bounds of what applicants consider early are unclear (see 112/2nd). The virus could also have the Ovalbumin promoter (Fig. 2A; Fig. 2C; Fig. 6B), which is magnum specific (claim 7). The technique described by Ivarie inherently results in expression specifically in the magnum as in claim 7 because the CMV promoter is a constitutive promoter and because cells in the magnum had the transgene in their genome (col. 8, lines 4-10). The CMV promoter is a "tissue specific promoter" (claim 6) because it provides expression of the exogenous protein in the egg white. The CMV promoter is also a promoter "specific for magnum tissue" (claim 7) because it is provides expression of the exogenous protein in the egg white and meets the definition of "magnum-specific" in col. 15, lines 48-52, of Ivarie and because cells in the magnum had the transgene in their genome (col. 8, lines 4-10). Claim 9 is included because the metes and bounds of a coding sequence that is "optimized form codon usage by a chicken" are unclear. Claim 10 and 24 are included because the virus had an IRES (Fig. 2F). Claims 11-13 and 25-27 are included because the virus encoded neo and gene X (Fig. 2A and 2F). Claims 14 and 28 are included because Ivarie taught the vector could encode an antibody (col. 19, lines 24-42). Thus, it would have been obvious to perform the methods claimed in '822 using the specific limitations now claimed based on the disclosure of '822. '822 did not teach the embryos were introduced into an oviduct of a recipient hen as required in claims 1 and 20 in the instant application.

However, Tanaka (1994, J. Reprod. Fert., Vol. 100, pg 447-449) taught delivering DNA to an embryo, then delivering the embryo to the oviduct of a recipient hen (pg 449, col. 1, last ¶). The embryo hatched and became a chick (pg 447, col. 2, "Materials and Methods;" pg 448, Fig. 1; pg 448, col. 1, line 4; pg 448, col. 2, 1st full ¶, line 9).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver virus encoding an exogenous protein under the control of the CMV promoter into an embryo by glass capillary and allow the embryo to become a chick as taught by '822 wherein the embryo was introduced into a recipient hen's oviduct as described by Tanaka. One of ordinary skill in the art at the time the invention was made would have been motivated to transplant the embryo of '822 into the oviduct of a recipient hen to provide the most natural environment for the embryo and to avoid artificial methods of incubating the embryo in media in a host shell.

Thus, Applicants' claimed invention as a whole is prima facie obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Harvey (Feb. 2002, Poultry Sci. Vol. 81, pg 202-212)

US Patent 6,573,097

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER